
Can Multiple Myeloma Be Cured Without Allogeneic SCT? Defending: **NO**

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Cure with Conventional Chemotherapy*

- Disappointingly small

(1 per 1,000)

*Kyle RA. Am J Hematol, 1988,
and personal communication

Cure with Allogeneic Stem-cell Transplantation?

Molecular Remission after Transplantation: ASCT vs “Allo”

| Procedure | N°. of Patients | PCR-negative |
|------------------|------------------------|---------------------|
| ASCT | 15 | 7% |
| Allo | 14 | 50% |

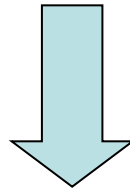
Allogeneic transplantation **Myeloablative** conditioning

Impact of Molecular Remission after Allogeneic Transplantation

| PCR status | N°. of Patients | Relapse rate at 5-years |
|----------------------|-----------------|-------------------------|
| Negative | 16 | 0% |
| Mixed pattern | 19 | 33% |
| Positive | 13 | 100% |

Myeloablative Allogeneic Transplantation

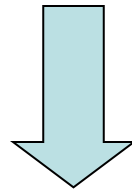
- High TRM
- High relapse rate



Cure rate \approx 10 – 15%

Dose-Reduced Intensity Conditioning

- Lower TRM
- Higher relapse rate



Controversial results

Double **ASCT** versus tandem **ASCT/Allo-RIC**

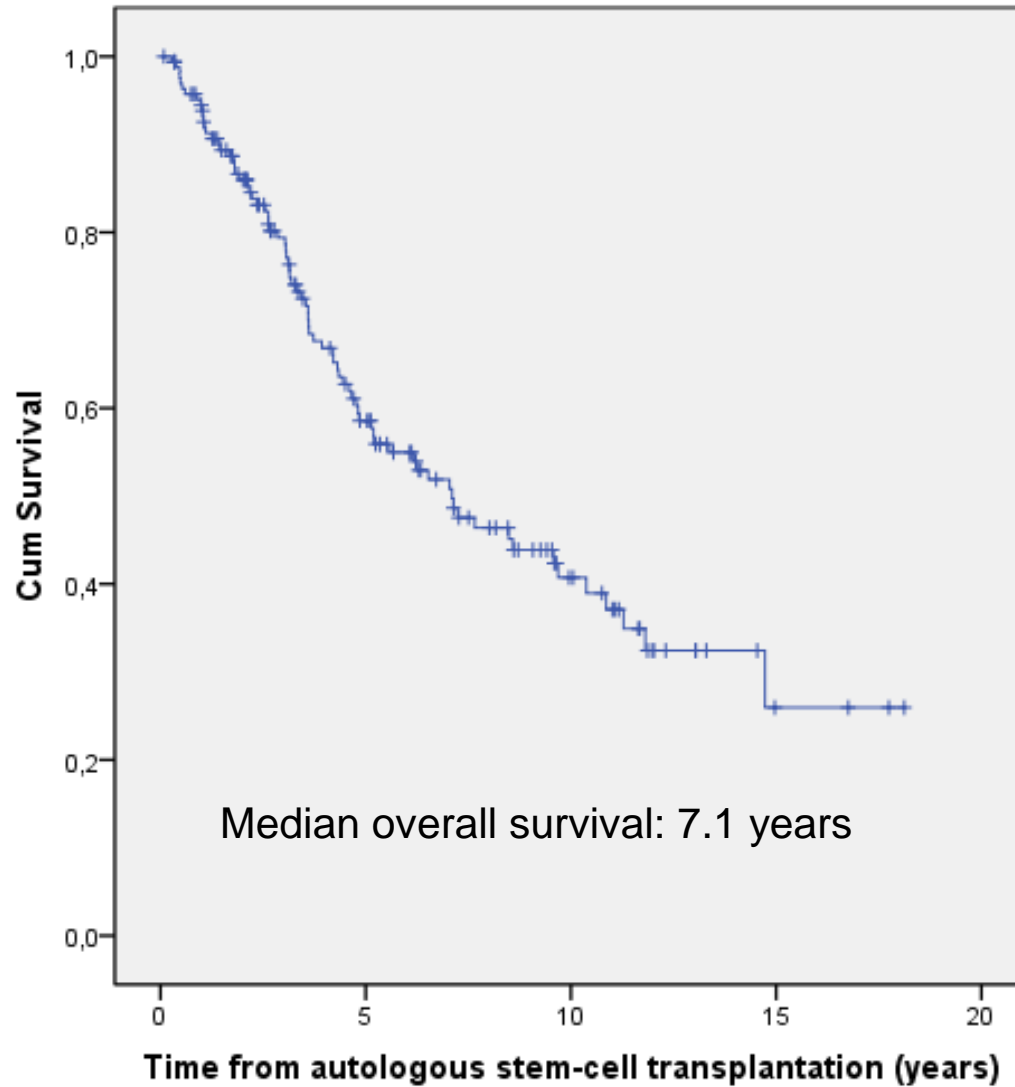
| Author | No. Pts | CR rate (%) | EFS mos. | OS mos. |
|---|------------|-----------------------|------------------------------------|------------------------------------|
| Garban <i>et al</i>, Blood 2006 | 166 vs 46 | 51 vs 62 (p=NS) | 35 vs 32 (p=NS) | 47 vs 35 (p=0.07) |
| Bruno <i>et al</i>, NEJM 2007&2009 | 82 vs 80 | 26 vs 55 (p=0.004) | 29 vs 35 (p=0.02) | 54 vs 80 (p=0.01) |
| Rosiñol <i>et al</i>, Blood 2008 | 85 vs 26 | 11 vs 40 (p=0.01) | 26 vs 19.6 (p=NS) | 58 vs NR (p=NS) |
| Knop <i>et al</i>, Blood 2009 | 73 vs 126 | 32 vs 59 (p=0.003) | - | 72% vs 60% (at 36 mos, p=NS) |
| Bjorkstrand <i>et al</i>, JCO 2011 | 249 vs 108 | 41 vs 51 (p=0.02) | 18% vs 35% (at 60 mos, p=0.001) | 58% vs 65% (at 60 mos, p=0.006) |
| Krishnan <i>et al</i>, Lancet Onc 2011 | 185 vs 397 | 35 vs 48 (p=0.009) | 46% vs 43% (at 3 yrs p=NS) | 80% vs 77% (at 3 yrs, p=NS) |

Double **ASCT** versus tandem **ASCT/Allo-RIC**

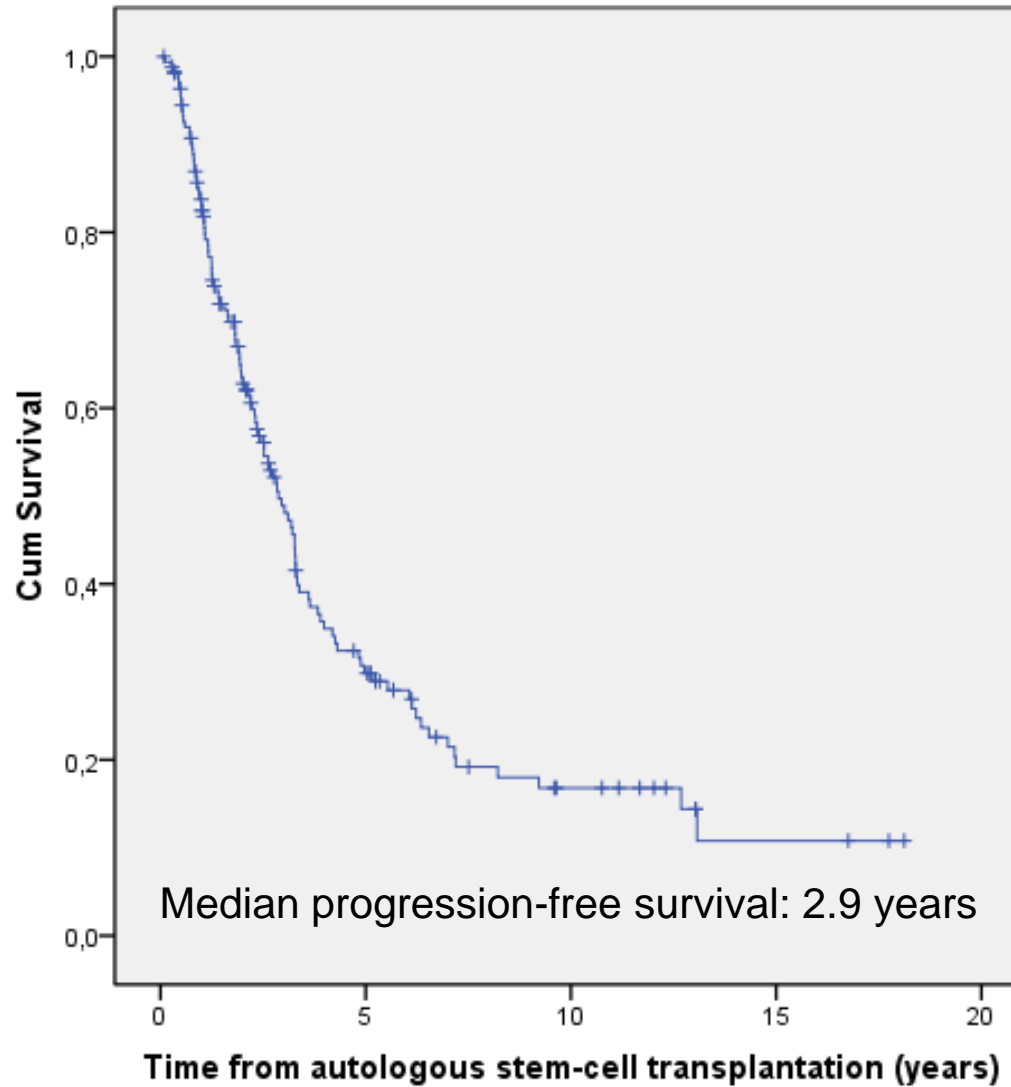
| Author | Patient Characteristics | Conditioning |
|---|--|--|
| Garban <i>et al</i>, Blood 2006 | High-risk (high β 2M, 13q-) | Fludarabine/ Busulphan/ ATG |
| Bruno <i>et al</i>, NEJM 2007 | All | TBI (2 Gys) |
| Rosiñol <i>et al</i>, Blood 2008 | No CR/nCR with 1 st transplant | Fludarabine/ MEL-140 |
| Knop <i>et al</i>, Blood 2009 | 13q- | Fludarabine/melphalan (+ATG in UNR) |
| Björkstrand <i>et al</i>, JCO 2011 | CR, PR, SD | Fludarabine/TBI (2 Gy) |
| Krishnan <i>et al</i>, Lancet Onc 2011 | CR, PR, SD | TBI (2 Gys) |

Can ASCT be Curative?

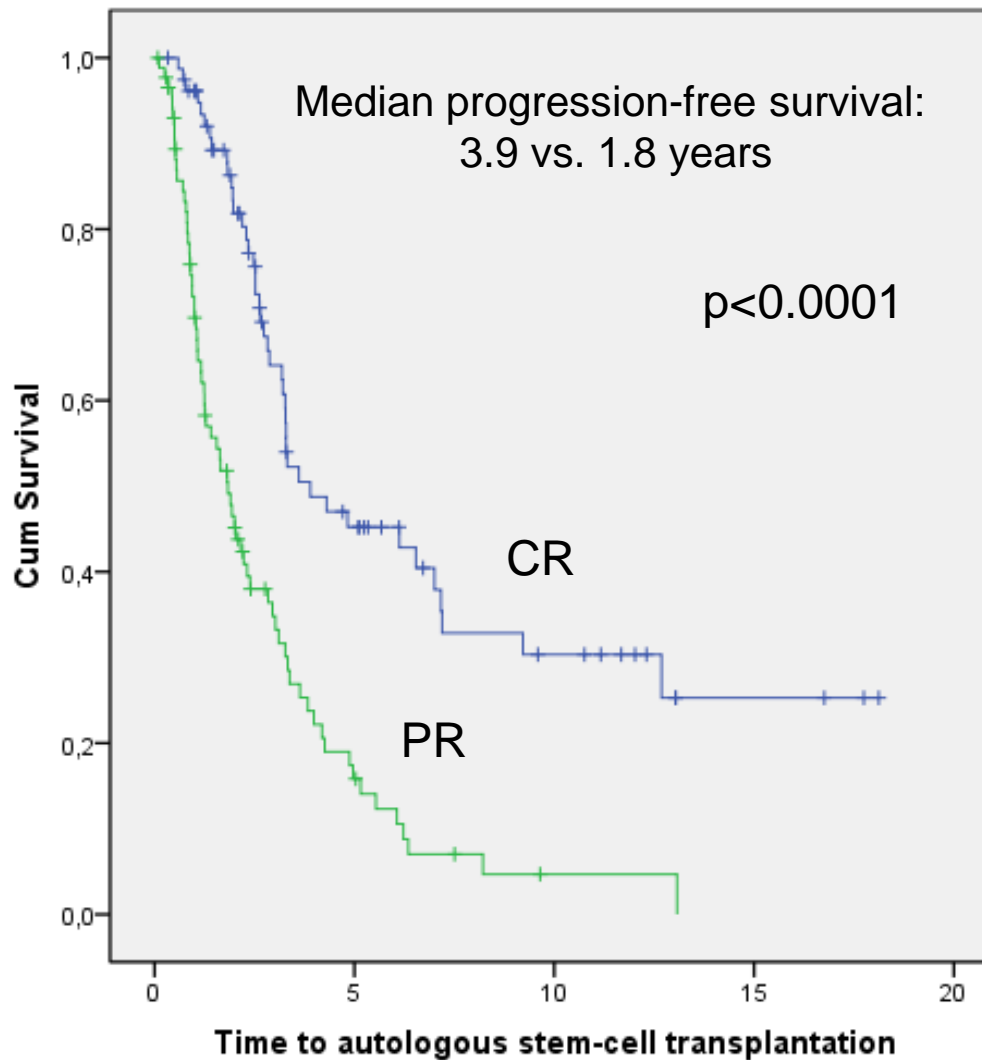
OS after front-line ASCT



PFS after front-line ASCT

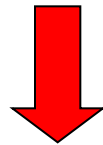


PFS according response to transplant (CR vs. PR)



Can ASCT be Curative?

- Arkansas Total Therapy I*
16/231 patients in continued CR after a median follow-up of 12 years
- Spanish Registry**
35% of patients in CR remain in CCR >10 years after ASCT
- Hospital Clínic***
9/167 patients in CCR from 10 to 18 years after ASCT



≈ 5 -10 % of patients in CCR beyond 10 years from ASCT

* Barlogie *et al.* BJH 2006; 135: 158-164

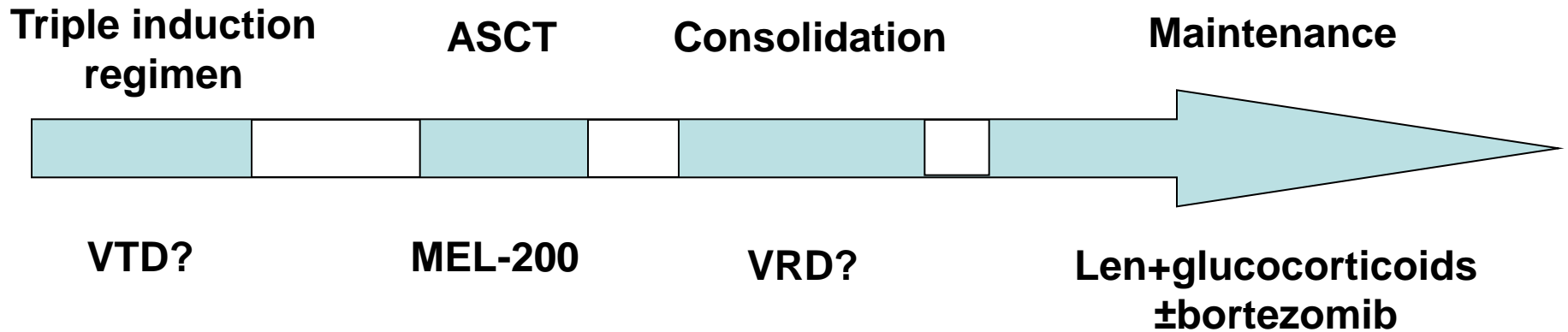
** López-Martínez *et al.* Blood 2011; 118: 529-534.

*** Hospital Clínic, Barcelona, 2012

Can the Cure Rate with ASCT be increased with the Incorporation of Novel Agents?

- Induction + ASCT → ?
 - Refined “Total Therapy” → Likely
-

Refined “Total Therapy”



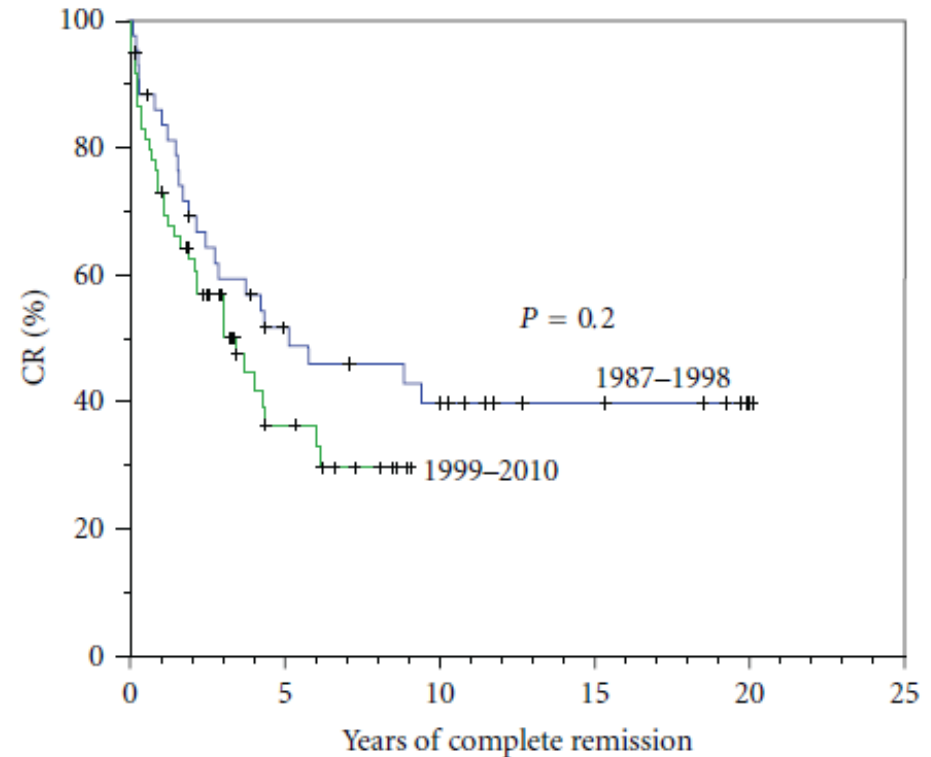
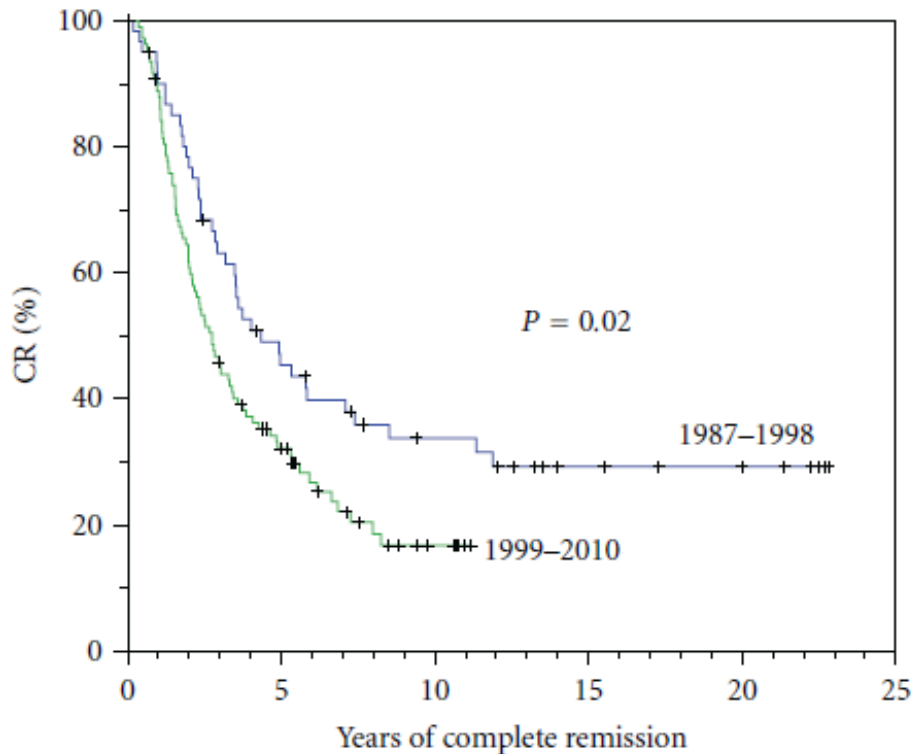
Curability of Multiple Myeloma

- 792 patients ≤ 65 years
- Diagnosis between 1987 – 2010
- 13 patients in continued CR > 12 years with no relapse



3% of all patients
22% of those in CR

Curability of Multiple Myeloma



* Alexanian *et al.* Bone Marrow Res 2012

Definition of cure in MM

Sustained negative IF
complete remission
> 10 years

Is Myeloma a Curable Disease?

- Conventional chemotherapy: 1 ‰
- ASCT: 5 -10%
- Allo-SCT: 10-20% ?
- ASCT plus current novel agents: ?



Need for targeted therapies to prevent progression

